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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,803	11/14/2005	Giuseppe Arpaia	279737US0PCT	1463

22850 7590 10/09/2009

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EXAMINER	
XU, XIAOYUN	
ART UNIT	**PAPER NUMBER**
1797	

NOTIFICATION DATE	DELIVERY MODE
10/09/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/556,803	ARPAIA ET AL.	
	Examiner	Art Unit	
	ROBERT XU	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-17,23 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-17,23 and 24* is/are rejected.

7)☒ Claim(s) *23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment and RCE filed on 09/09/2009 have been entered and fully considered. Claim 22 is canceled. Claims 15-17, 23 and 24 are pending, of which Claims 15, 23 and 24 are amended.

Response to Amendment

2. In response to amendment, the examiner maintains rejection over the prior art established in the previous Office action.

Claim Objections

3. Claim 23 is objected to because of the following informalities: Claim 23 recites "100 pg/ml". The correct word should be "100 µg/ml", because only 100 µg/ml of Pluronic F68 is supported by the specification (see page 11, line 20). Appropriate correction is required.

Claim Rejections - 35 USC § 103

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. **Claims 15 -17 and 23** are rejected under 35 U.S.C. 103(a) as being unpatentable over Katakam et al. (Pharmaceutical Development and Technology, 1997) (Katakam) in view of Wu (Journal of Endocrinology, 1993).

In regard to Claim 15, Katakam teaches the use of Poloxamer polymer to stabilize recombinant human growth hormone (rhGH) against various processing stress (see title). The method comprises:

mixing the protein sample (rhGH) by adding a Poloxamer 188 (Pluronic F68) to the sample (see page 144, left col. 3rd paragraph, Table 1);

performing chromatography (size exclusion column- HPLC) on the protein sample (see page 145, right col. 1st paragraph); and

the quantity of the total protein is determined by UV absorbance of the eluted protein solution (see page 145, right col. 1st paragraph and Figure 1-2).

Katakam does not specifically teach using data from calibration with a standard to calculate the quantity of the protein. However, using data from calibration with a standard to calculate the quantity of the protein is well known in the art. At time of the invention, it would have been obvious for a person of ordinary skill in the art to use data from calibration with a standard to calculate the quantity of the protein.

Katakam does not teach FSH. Wu teaches that FSH from bovine pituitary glands is isolated by size exclusion (gel filtration) chromatography (see abstract). Since Katakam demonstrates that Poloxamer reduces aggregation of HGH, it would have been obvious to one of ordinary skill in the art to apply the same method on other proteins. From particular to general is how science and engineering developed.

In regard to Claim 16, simple dilution of protein sample to a level acceptable for the chromatographic system is well-known in the art.

In regard to Claim 17, Katakam teach using size-exclusion chromatography (SEC) to quantify protein (see page 145, right col. 1st paragraph).

In regard to Claim 23, Katakam tests various concentrations of Poloxamer 188 (Pluronic 68) in the range from 0.001% (below cmc) to 0.2% (above cmc) (see Table 1). The concentration of 100 µg/ml is equivalent to 0.01%. Katakam's teaching meets the recited limitation.

6. **Claim 24** is rejected under 35 U.S.C. 103(a) as being unpatentable over Katakam in view of Wu as applied to Claim 15 above, and further in view of Toschi (European Journal of Biochemistry, 1998).

In regard to Claim 24, Katakam teaches that the most effective concentration of Poloxamer is above cmc, or up to 0.2% (see page 146, left col. 1st paragraph). Katakam does not teach that Poloxamer 188 (Pluronic 68) is added in sodium acetate buffer at pH 3.8 in the protein solution. Toschi teaches that elution buffer of 0.01% Poloxamer 188 (Pluronic 68) and 50 mM sodium acetate, pH 4 is used in protein purification by chromatography (see page 109, left col., lines 28-33). Toschi does not teach that elution buffer comprises 0.1% Poloxamer 188 (Pluronic 68). The court has held that differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is

critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." (In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)). Toschi teaches the concentration of Poloxamer 188 (Pluronic 68) is 0.01% and Katakam teaches the most effective concentration of Poloxamer 188 (Pluronic 68) is up to 0.2%. It would have been obvious for a person of ordinary skill in the art to optimize the concentration of Poloxamer 188 (Pluronic 68) in protein solution to be 0.1% by routine experimentation.

Response to Arguments

7. Applicant's arguments filed 09/09/2009 have been fully considered but they are not persuasive.

Applicant argues that HGH and FSH are very different proteins, having remarkably different structures. Therefore, how one protein (HGH) acts in a given set of experiments (like in Katakam) provides no reasonable guidance as to how a second, distinct protein (FSH from Wu) would behave. Since Katakam demonstrates that Poloxamer reduces aggregation of HGH, it would have been obvious to one of ordinary skill in the art to apply the same method on other proteins. From particular to general is how science and engineering develop. For example, there is a report on using Poloxamer 188 to increase the post-thaw growth of cryopreserved plant cells (Cryobiology, 1996).

Applicant's notation that "Table 1 (page 147) in Katakam clearly shows that Poloxamer 188 was the worst stabilizer among those tested" is acknowledged. Katakam teaches that at the concentration of CMC or lower, Poloxamer 188 was the worst stabilizer among those tested (see Table 1). However, at concentration above CMC (0.2%), all stabilizers performed the same (see page 146, left col. 1st paragraph, page 147, Table 1). As a matter of fact, 100 µg/ml of Poloxamer 188 recited in Claim 23 is over twice amount of CMC of Poloxamer 188, and 0.1% of Poloxamer 188 recited in Claim 24 is over 20 times of CMC of Poloxamer 188. Since Poloxamer 188 is a widely used surfactant in the art, it would have been economical to try Poloxamer 188 first.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT XU whose telephone number is (571)270-5560. The examiner can normally be reached on Mon-Thur 7:30am-5:00pm, Fri 7:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on (571)272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

10/6/2009

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

RX